Effective Regurgitant Orifice Area: A Noninvasive Doppler Development of an Old Hemodynamic Concept

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Objectives. The purpose of this study was to determine the feasibility, relation to other methods and significance of the effective regurgitant orifice area measurement.

Background. Assessment of the severity of valvular regurgitation (effective regurgitant orifice area) has not been implemented in clinical practice but can be made by Doppler echocardiography.

Methods. Effective regurgitant orifice area was calculated by Doppler echocardiography as the ratio of regurgitant volume/regurgitant jet time-velocity integral and compared with color flow Doppler mapping, angiography, surgical classification, regurgitant fraction and variables of volume overload.

Results. In 210 consecutive patients examined prospectively, feasibility improved from the early to the late experience (65% to 95%). Effective regurgitant orifice area was 28 ± 23 mm^2 (mean ± SD) for aortic regurgitation (32 patients), 22 ± 13 mm^2 for ischemic/functional mitral regurgitation (50 patients) and 41 ± 32 mm^2 for organic mitral regurgitation (82 patients). Significant correlations were found between effective regurgitant orifice and mitral jet area by color flow Doppler mapping (r = 0.68 and r = 0.63, $p < 0.0001$, respectively) and angiographic grade (r = 0.77, p = 0.0004). Effective regurgitant orifice area in surgically determined moderate and severe lesions was markedly different in mitral regurgitation (35 ± 12 and 75 ± 33 mm^2, respectively, p = 0.009) and in aortic regurgitation (21 ± 8 and 38 ± 5 mm^2, respectively, p = 0.08). Strong correlations were found between effective regurgitant orifice area and variables reflecting volume overload. A logarithmic regression was found between effective regurgitant orifice area and regurgitant fraction, underlining the complementarity of these indexes.

Conclusions. Calculation of effective regurgitant orifice area is a noninvasive Doppler development of an old hemodynamic concept, allowing assessment of the lesion severity of valvular regurgitation. Feasibility is excellent with experience. Effective regurgitant orifice area is an important and clinically significant index of regurgitation severity. It brings additive information to other quantitative indexes and its measurement should be implemented in the comprehensive assessment of valvular regurgitation.

(J Am Coll Cardiol 1994;23:443–51)

Assessment of the severity of valvular regurgitation with both invasive and noninvasive techniques is widely used but remains essentially semiquantitative, and interpretation frequently leaves room for uncertainty (1). By contrast, in valvular stenoses, quantitative measures of severity (2) are now the rule, and noninvasive measurement of the mitral (3,4) or aortic (5,6) stenotic valve area has greatly facilitated follow-up of patients. By analogy, in valvular regurgitation, it would be desirable to evaluate not only the volume overload by measuring the regurgitant volume but also the severity of the lesion by measuring the effective regurgitant orifice area.

For this purpose, 40 years ago Gorlin and Dexter (7) described the principle of calculation of the mitral regurgitant orifice area. Unfortunately, its implementation was almost impossible, and subsequently the effective regurgitant orifice area calculation utilizing various formulas and methods appeared in scattered reports but remained an elusive concept.

However, simple hydrodynamic principles readily applicable to Doppler echocardiography can be used to measure the effective regurgitant orifice area. In the absence of a previously validated reference, the effective regurgitant orifice area calculation was prospectively performed to determine its feasibility, relation to other methods and clinical significance.

Methods

Patients were included prospectively and were examined in 1991 in our laboratory by one of us and represent our consecutive experience. Inclusion criteria were 1) presence of pure, isolated mitral or aortic regurgitation of at least mild degree, as determined by standard two-dimensional Doppler color flow imaging; 2) complete two-dimensional echocardiographic and Doppler measurements allowing quantitation

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Manuscript received March 29, 1993; revised manuscript received September 10, 1993, accepted September 30, 1993.

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0735-1097/94/$7.00

of mitral or aortic regurgitation; and 3) clear delineation of the jet velocity envelope by continuous wave Doppler echocardiography. The 210 patients meeting criterion 1 were screened. Six patients did not meet criterion 2 because of technical factors, and 40 did not meet criterion 3. The remaining 164 patients formed our study group. Their mean age was 65 ± 13 years; 95 were men, and 69 were women; 128 were in sinus rhythm, and 36 were in atrial fibrillation. Of the 164 patients, 32 had isolated aortic regurgitation, 50 had isolated mitral regurgitation classified as functional or due to ischemic disease, or both, as previously described (8,9) and 82 had isolated mitral regurgitation of organic cause.

The accuracy of the quantitative Doppler method was assessed as follows: 1) 23 additional patients with completely normal results on Doppler echocardiographic examination were used as control subjects for quantitative Doppler values and for normal left ventricular and atrial measurements; and 2) 12 patients with regurgitation were studied by two observers during the same examination to assess interobserver variability.

Theoretical basis. For any given orifice traversed by a fluid (10), flow is determined by

$$\text{Flow} = \text{Orifice area} \times \text{Velocity}. \qquad [1]$$

For a regurgitant orifice it becomes

$$\text{Regurgitant flow} = \text{Regurgitant orifice area} \times \text{Regurgitant velocity}. \qquad [2]$$

Integrated over the regurgitant period,

$$\int \text{Regurgitant flow} = \text{Regurgitant orifice area} \times \int \text{Regurgitant velocity}, \qquad [3]$$

where

$$\int \text{Regurgitant flow} = \text{Regurgitant volume}; \qquad [4]$$

$$\int \text{Regurgitant velocity} = \text{Regurgitant time-velocity integral}; \qquad [5]$$

and thus,

$$\text{Effective regurgitant orifice} = \text{Regurgitant volume/Regurgitant time-velocity integral} \qquad [6]$$

(the numerator and denominator of the right side of equation 6 can be obtained by Doppler echocardiography).

Doppler echocardiographic analysis. All patients had a complete two-dimensional echocardiographic and Doppler study using multiple windows, as previously described (11,12), with a Hewlett-Packard or Acuson phased-array system equipped with a 2.5-MHz transducer. Quantitative Doppler measurements and calculations were performed on-line at the time of the study.

Quantitative Doppler study: data collection. Quantitative Doppler study was performed as previously described (13,14). The diameters of the aortic annulus in systole and the mitral annulus in diastole were measured at the point of insertion of the leaflets (inner edge). The apical four-chamber view was used to record and digitize the pulsed wave Doppler signal at the mitral and aortic annuli, and the time-velocity integrals were computed (Fig. 1A and 2A). At least three measurements of each variable were averaged (six for patients in atrial fibrillation).

Continuous wave Doppler echocardiography was recorded with an apical or para-apical window to obtain the maximal velocities of the regurgitant jet, either guided by color flow imaging or utilizing a nonimaging transducer. Maximal sweep speed and wall filter settings were used. Once the full envelope was obtained, the outline (maximal spectral signal velocity) was digitized, and the time-velocity integral of the regurgitant jet was computed (Fig. 1B and 2B).

Calculations. The cross-sectional areas of the mitral and aortic annuli were calculated with the πR^2 formula, assuming a circular shape. The mitral and aortic stroke volumes were obtained by multiplying the cross-sectional area by the respective time-velocity integral determined by pulsed wave Doppler imaging at each specific location.

The regurgitant volume was calculated as

$$\text{Regurgitant volume} = |\text{Mitral stroke volume} - \text{Aortic stroke volume}|.$$

The regurgitant fraction was calculated as

$$\text{Regurgitant fraction} = \text{Regurgitant volume/Mitral or aortic stroke volume}.$$

The effective regurgitant orifice was calculated as

$$\text{Effective regurgitant orifice} = \text{Regurgitant volume/Regurgitant time-velocity integral}.$$

Color flow imaging. In patients with mitral regurgitation, quantitative analysis of color flow imaging was performed off-line. Two orthogonal planes were obtained (the four-chamber view and the two-chamber or long-axis view), and the average of the two views was used for calculation of jet area (15,16).

Physiologic variables. The left ventricular volumes were measured at end-diastole and end-systole with the biapical (four- and two-chamber) Simpson rule (method of disks), as recommended by the American Society of Echocardiography (17), and indexed to body surface area.

The left atrial volumes were measured in normal patients and in patients with mitral regurgitation with the use of two orthogonal apical views (18,19). Cardiac output was calculated by multiplying the heart rate by the stroke volume of the nonregurgitant valve (13). The systolic pulmonary artery

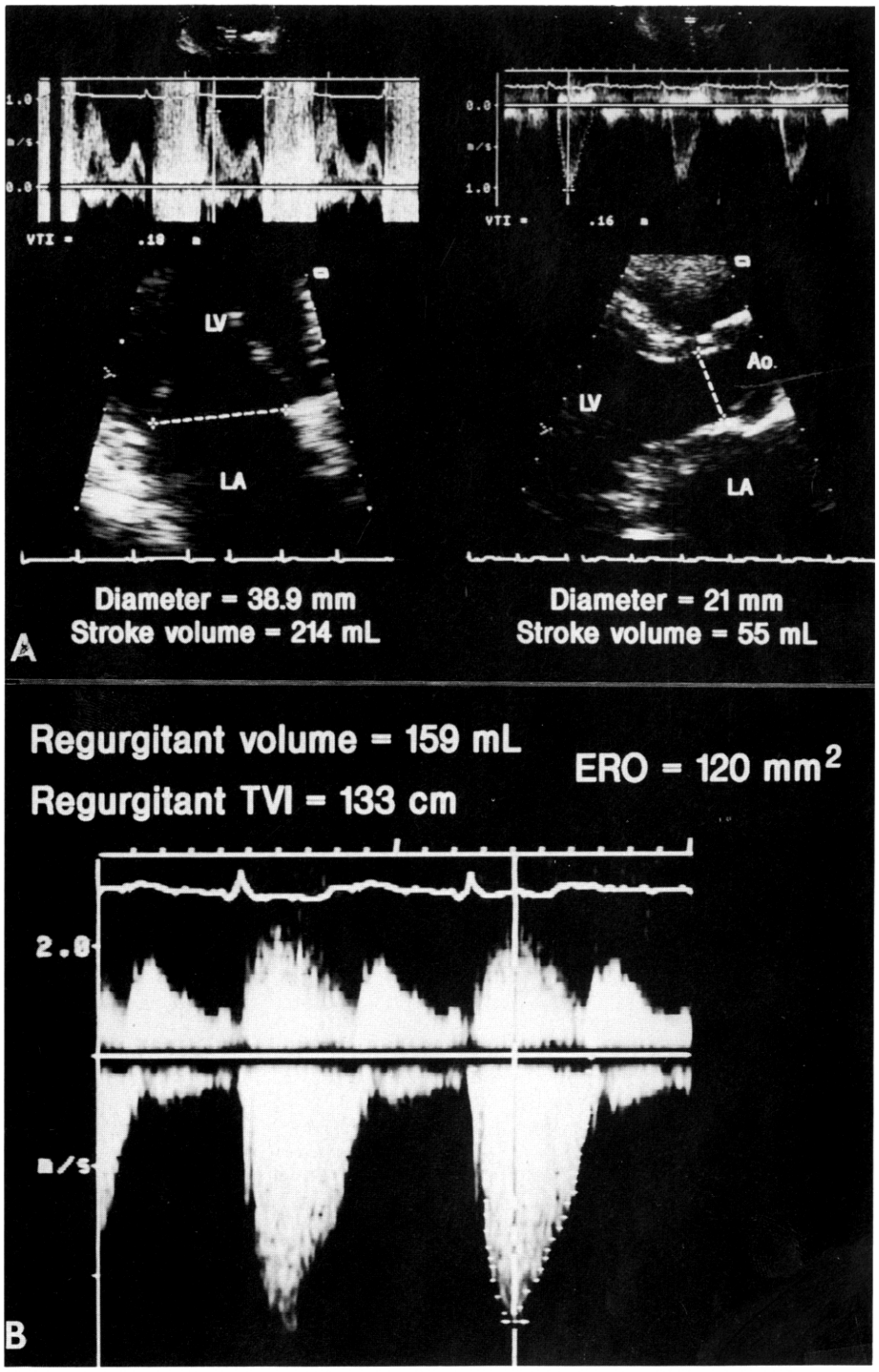


Figure 1. Example of measurement of effective regurgitant orifice area in a patient with mitral regurgitation. **A,** Measurement of the regurgitant volume with pulsed wave Doppler two-dimensional echocardiography. **Left,** Mitral measurement (38.9-mm diameter, 214-ml stroke volume). **Right,** Aortic measurement (21-mm diameter, 55-ml stroke volume). Ao = aorta; LA = left atrium; LV = left ventricle. **B,** Continuous wave Doppler signal of mitral regurgitation. Outline of regurgitant signal is traced, and regurgitant time-velocity integral (VTI) is calculated. Effective regurgitant orifice = 120 mm^2, regurgitant volume = 159 ml, regurgitant time-velocity integral = 133 cm.

pressure was estimated by using the maximal tricuspid regurgitation velocity (20).

Surgical and angiographic analysis. The indication for surgical correction of the valvular regurgitation was determined by the attending physicians. Surgical inspection of the valve was performed in 28 patients (17%) (22 with mitral and 6 with aortic regurgitation) and regurgitation was classified as mild, moderate or severe.

The decision to request angiography was made at the discretion of the patient's primary cardiologist. The angiographic results were classified in four grades (21). Of the 28 surgical patients, 24 (86%) underwent coronary angiography and 12 (43%) underwent selective angiography (left ventriculography in 10, aortography in 2). An additional six nonsurgically treated patients underwent left ventriculography. Thus, a total of 18 patients had angiographic assessment of regurgitation (16 mitral, 2 aortic) available for comparison with the calculation of effective regurgitant orifice area.

Statistical analysis. Descriptive group results were expressed as mean value ± SD. Groups were compared with

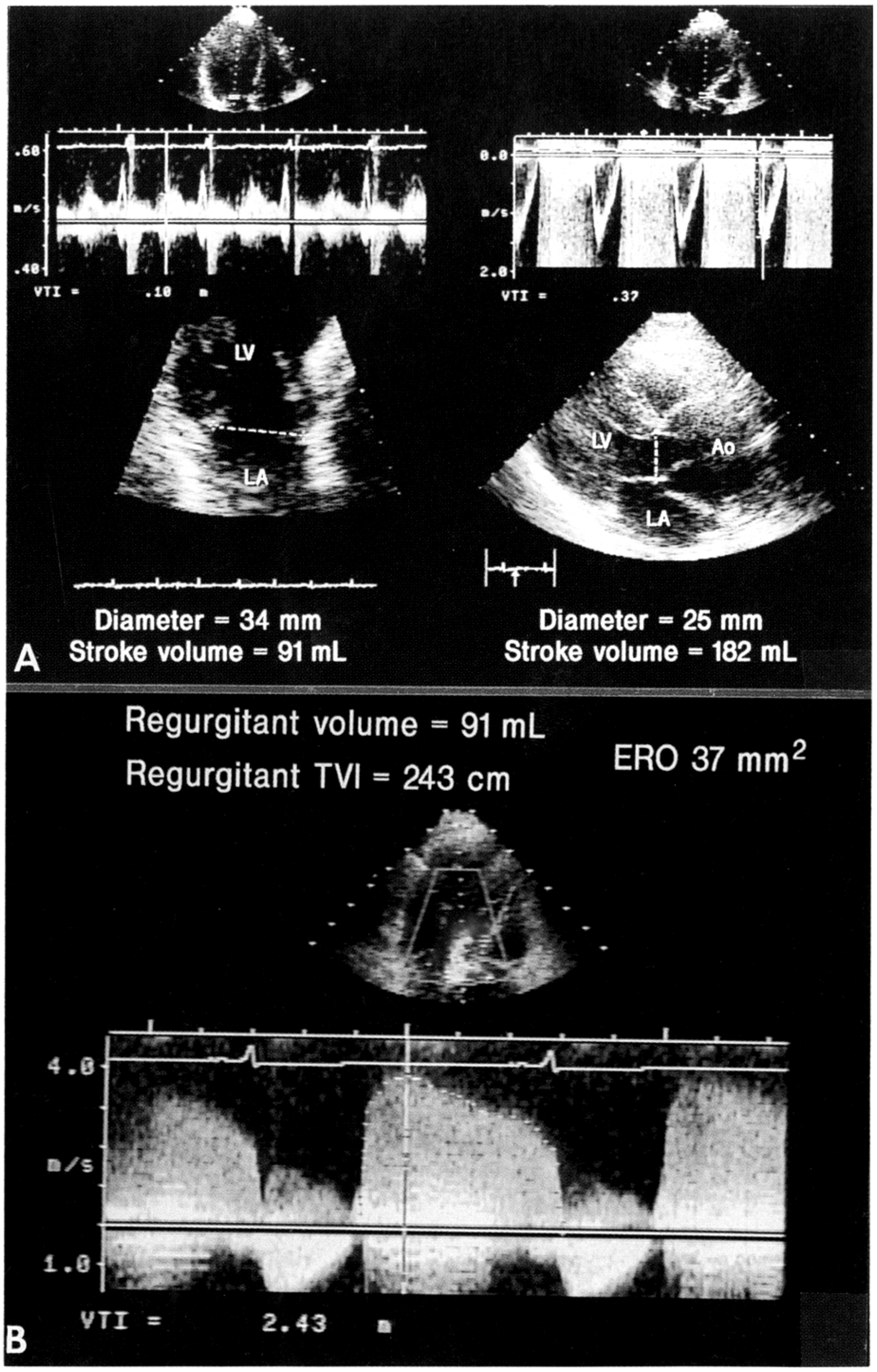


Figure 2. Example of calculation of effective regurgitant orifice in a patient with aortic regurgitation. **A,** Calculation of regurgitant volume with pulsed wave Doppler two-dimensional echocardiography. **Left,** Mitral measurement (34-mm diameter, 91-ml stroke volume). **Right,** Aortic measurement (25-mm diameter, 182-ml stroke volume). Abbreviations as in Figure 1. **B,** Continuous wave Doppler signal of aortic regurgitation. Outline of continuous wave Doppler signal is traced, and regurgitant time-velocity integral (VTI) is obtained. Effective regurgitant orifice = 37 mm^2; regurgitant volume = 91 ml; regurgitant time-velocity integral = 243 cm.

the Student *t* test. Effective regurgitant orifice area was related to color flow and physiologic variables with linear regression. The relation to angiographic severity was assessed by Pearson rank correlation. Effective regurgitant orifice area was related to regurgitant fraction by linear correlation after transforming to the logarithm of effective regurgitant orifice area. Comparison of rates of feasibility was based on the chi-square test. Comparison of effective regurgitant orifice area in subgroups defined by the surgical assessment was based on the Wilcoxon rank-sum test.

Results

Regurgitation variables are summarized in Table 1. The average effective regurgitant orifice area was 28 mm^2 (range 4 to 84) in aortic regurgitation, 22 mm^2 (range 5 to 64) in ischemic/functional mitral regurgitation and 41 mm^2 (range 2 to 139) in organic mitral regurgitation.

Feasibility and reproducibility. The feasibility of the technique (164 of 210 patients) is presented in Table 2. The feasibility for regurgitant volume measurement was high,

Table 1. Measurements of Regurgitation in 164 Patients With Aortic or Mitral Regurgitation

		Mitral Regurgitation	
	Aortic Regurgitation (n = 32)	Ischemic/ Functional (n = 50)	Organic (n = 82)
Regurgitant volume (ml)	58 ± 43	29 ± 13†	60 ± 43**
Regurgitant fraction (%)	37 ± 16	33 ± 11	41 ± 19*
Regurgitant TVI (cm)	226 ± 45	148 ± 36††	157 ± 31††
Regurgitant orifice (mm^2)	28 ± 23	22 ± 13	41 ± 32†**

*p < 0.02 (†) and p = 0.0001 (††) compared with aortic regurgitation group. p < 0.003 (*) and p = 0.0001 (**) compared with group that had ischemic or functional mitral regurgitation. Values presented are mean value ± SD. TVI = time-velocity integral.

Table 2. Feasibility of Quantitative Doppler and Regurgitant Orifice Calculation in the Overall Group of Patients With Aortic or Mitral Regurgitation and Three Subgroups

	Early Experience		Late Experience	
	No. Completed/ No. Attempted	%	No. Completed/ No. Attempted	%
Quantitative Doppler	100/105	95	104/105	99
Regurgitant orifice				
Overall group	65/100	65	99/104	95
Subgroups				
Aortic regurgitation	11/19	58	21/21	100
Mitral regurgitation				
Ischemic/functional	20/24	83	30/30	100
Organic	34/57	60	48/53	91

between 95% and 99%, and improved markedly over time for effective regurgitant orifice area calculation, from 65% to 95% ($p < 0.001$). In the late phase, we could not obtain the full envelope of the jet of organic mitral regurgitation in 5 (9%) of 53 patients, either because of mild regurgitation with a very weak or incomplete continuous wave Doppler signal or because of a markedly eccentric jet.

With regard to the interobserver variability, excellent correlations were found between Observers 1 and 2 for regurgitant time-velocity integral ($r = 0.97$, $p < 0.0001$, SEE 7 cm) and effective regurgitant orifice area ($r = 0.98$, $p < 0.0001$, SEE 9 mm^2). In the 23 normal patients, the regurgitant volume was 4 ± 4 ml, and the regurgitant fraction was 4.5 ± 4%.

Effective regurgitant orifice and other methods of assessing regurgitation. *Color flow Doppler imaging.* The correlations between the effective regurgitant orifice area and the color flow Doppler jet area in patients with mitral regurgitation were significant: $r = 0.68$ and $p < 0.0001$ in ischemic/functional mitral regurgitation and $r = 0.63$ and $p < 0.0001$ in organic mitral regurgitation (Fig. 3).

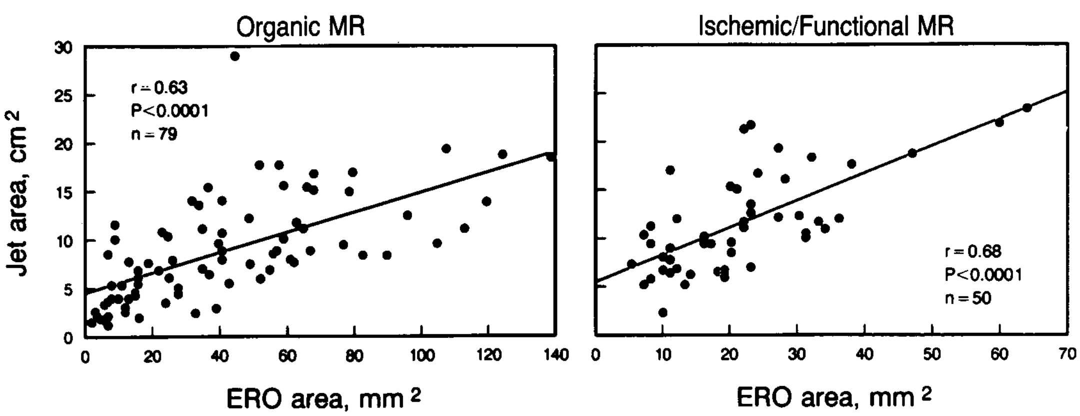
Angiography. In patients with mitral regurgitation, there was a significant correlation between angiographic grading and effective regurgitant orifice area: $r = 0.77$, $p = 0.0004$ (Fig. 4).

Surgical assessment. Effective regurgitant orifice area according to the subsets defined by the surgical classification was 35 ± 12 mm^2 in moderate and 75 ± 33 mm^2 in severe mitral regurgitation ($p = 0.009$) and 21 ± 8 mm^2 in moderate and 38 ± 5 mm^2 in severe aortic regurgitation ($p = 0.08$). There was minimal overlap between groups (Fig. 5).

Effective regurgitant orifice area and other quantitative indexes. *Regurgitant fraction.* As expected, a strong correlation was found between effective regurgitant orifice area and regurgitant fraction ($r = 0.95$, $p < 0.0001$), but the relation, identical for the three groups, was logarithmic (Fig. 6), showing the complementarity of these two indexes. For regurgitant fractions >40%, the relation became almost flat, and the wide range of severity of regurgitation was delineated in greater detail by the effective regurgitant orifice area.

Regurgitant volume. The scattering of regurgitant time-velocity integral values (95% confidence interval is 87 to 220 cm in mitral regurgitation and 137 to 315 cm in aortic

Figure 3. Correlations between effective regurgitant orifice (ERO) area and color flow Doppler jet area in patients with organic **(left)** and ischemic/functional **(right)** mitral regurgitation.



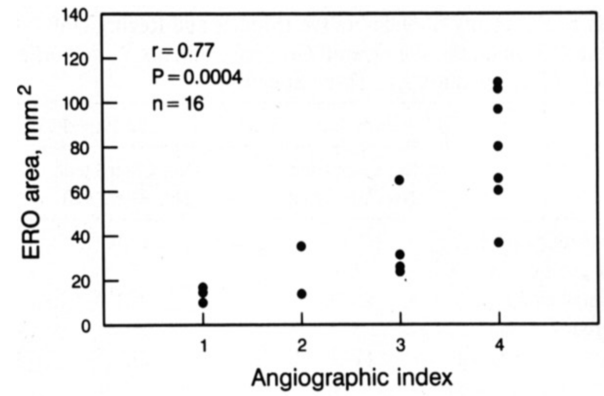


Figure 4. Correlation between angiographic severity of mitral regurgitation and effective regurgitant orifice (ERO) area.

regurgitation) was such that for any given regurgitant volume, a wide range of effective regurgitant orifice area could be calculated, underscoring the additive information provided by this variable.

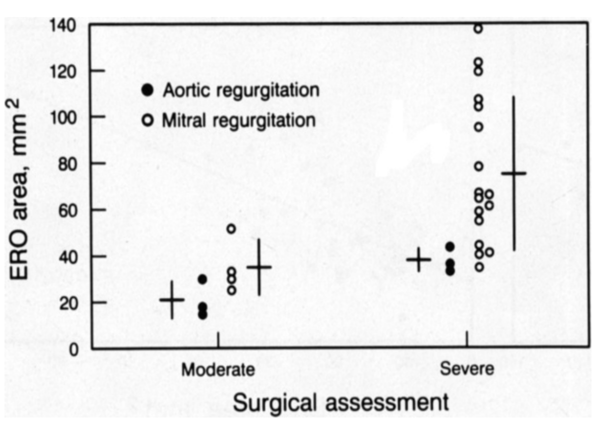
Hemodynamic measurements of volume overload. No significant correlations were found between the effective regurgitant orifice area and ejection fraction, cardiac output or cardiac index in any group.

Aortic regurgitation. In patients with aortic regurgitation, the effective regurgitant orifice area showed strong correlations with the left ventricular end-diastolic and end-systolic volume indexes ($r = 0.85$ and $r = 0.66$, respectively, $p < 0.0001$) (Fig. 7).

Organic mitral regurgitation. In patients with organic mitral regurgitation, the effective regurgitant orifice area showed significant but weak correlations with the left ventricular end-systolic volume index and systolic pulmonary artery pressure ($r = 0.38$, $p < 0.0004$ and $r = 0.31$, $p = 0.012$, respectively). Strong correlations were found between the effective regurgitant orifice area and the left ventricular end-diastolic volume index ($r = 0.70$, $p < 0.0001$) and between the effective regurgitant orifice area and the left atrial volume ($r = 0.74$, $p < 0.0001$) (Fig. 8).

Ischemic/functional mitral regurgitation. In patients with ischemic/functional mitral regurgitation, the effective regurgitant orifice area showed significant correlations with systolic pulmonary artery pressure and left atrial volume ($r = 0.43$, $p = 0.005$ and $r = 0.48$, $p = 0.0005$, respectively) (Fig. 9).

Figure 5. Surgical assessment of severity of valve lesion and effective regurgitant orifice (ERO) area in patients with mitral and aortic regurgitation. **Horizontal and vertical bars,** respectively, are mean value ± SD. Note the limited overlap between groups.



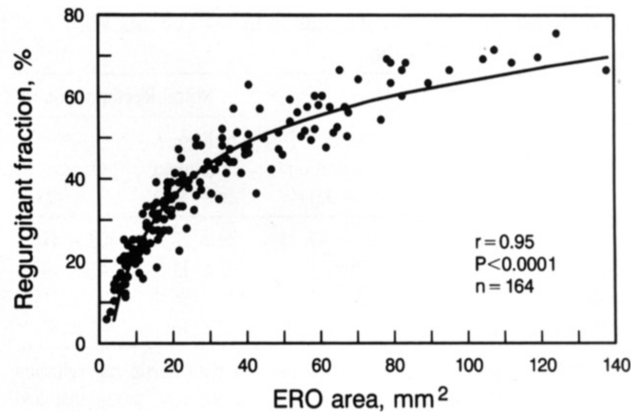


Figure 6. Correlation between effective regurgitant orifice (ERO) area and regurgitant fraction. The relation was curvilinear and became almost flat for regurgitant fractions >40%. Note the scattering of points, especially between regurgitant fractions of 40% to 50%, which underlines the complementarity of both indexes of severity of regurgitation.

Discussion

The possibility of noninvasively calculating the effective regurgitant orifice in a large number of patients with isolated aortic or mitral regurgitation represents a new Doppler development of an old hemodynamic concept.

Effective regurgitant orifice area: previous attempts at calculation. The principle of calculating effective orifice area described in 1952 by Gorlin and Dexter (7) had practical limitations and was seldom used (22,23). Experimental measurements using the same principle allowed a better understanding of mitral (24–28) and aortic regurgitation (29,30). Clinical studies were scarce for organic mitral (7,22) and aortic (31) regurgitation. More attention was devoted to functional mitral regurgitation by Keren et al. (32–35), who clarified important pathophysiologic points. However, the number of their patients was small, and the methodology was nonuniform. These variations, as well as the paucity of the data, probably explain why the effective regurgitant orifice area has remained an elusive concept. On the basis of the same hydrodynamic principle used for invasive determination of orifice area (36), the formula we used can be consistently applied in isolated regurgitation of any type. It integrates flow and velocity during the entire cardiac cycle and thus may differ slightly from the instantaneous effective regurgitant orifice area (25,37), but it represents the overall integrated severity of the lesion.

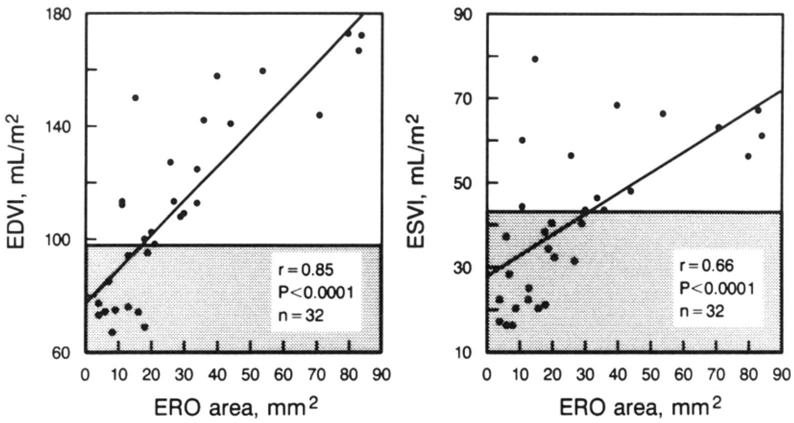


Figure 7. Aortic regurgitation. Correlation between effective regurgitant orifice (ERO) area and end-diastolic (EDVI) and end-systolic (ESVI) volume indexes. **Gray zone** indicates the upper range of normal values in 23 normal patients. Note that with increasing effective regurgitant orifice area, ventricular volumes increased.

Feasibility. The feasibility, relatively low in the early experience because of difficulties in obtaining the full jet envelope (38), increased to acceptable levels with a continued effort (thorough search for a complete, clean continuous wave Doppler jet signal); therefore, the effective regurgitant orifice area could be calculated in a large number of patients.

Effective regurgitant orifice area as an index of severity of regurgitation. The value of any individual method of assessment of regurgitation may be discussed, but the coherence of the relations between the effective regurgitant orifice area and 1) surgical assessment, 2) other methods of assessment of the severity of regurgitation, and 3) measurements of volume overloading underline its value as an index of severity of regurgitation. The significant but less than optimal correlations obtained with color flow Doppler jet area and left ventricular angiography are not surprising (39). Most important, it is now feasible to comprehensively assess noninvasively not only the volume overload (regurgitant volume and fraction) but also the severity of the valvular lesion itself (effective regurgitant orifice).

Comparison with other quantitative indexes. The regurgitant fraction is an accepted index of the severity of regurgitation. However, the curvilinear (logarithmic) regression between regurgitant fraction and effective regurgitant orifice area shows that for regurgitant fractions >40%, the relation becomes almost flat, and the wide range of lesion severity is more fully delineated by the effective regurgitant orifice area. The range of regurgitant time-velocity integral values shows that a wide range of effective regurgitant orifice area may be calculated for any given regurgitant volume.

Furthermore, the effective regurgitant orifice area also has theoretic advantages. Experimental (26,27,29,30) and clinical (33–35) data indicate that the degree of regurgitation is variable with hemodynamic manipulations, but the effective regurgitant orifice area is usually less variable (26,29,30), is not affected by heart rate (28) and may also help define the severity of acute regurgitation (40). These data underscore that the effective regurgitant orifice area provides complementary information to the regurgitant volume and fraction in assessment of the severity of valvular regurgitation and argue in favor of their combined use.

Clinical significance. The relation between effective regurgitant orifice area and the variables of volume overload demonstrates the strong immediate clinical significance of effective regurgitant orifice area. Individual variations are expected, probably due to variations in compliance of the cavities (41), in ventricular function (42) or in pressures (29,30).

In contrast to findings on valvular stenoses, the data are unclear about the definition of severe valvular regurgitation (43). In our series, an effective regurgitant orifice area >25 to 30 mm^2 in aortic regurgitation or >35 to 40 mm^2 in mitral

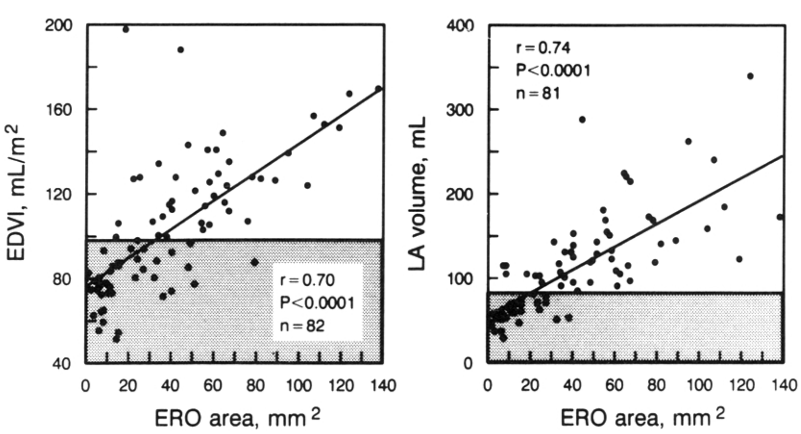


Figure 8. Organic mitral regurgitation. Correlation between effective regurgitant orifice (ERO) area and end-diastolic volume index (EDVI) and left atrial (LA) volume. **Gray zone** indicates the upper limit of normal range in 23 normal patients. Note that with increasing effective regurgitant orifice area, ventricular and left atrial volumes increased.

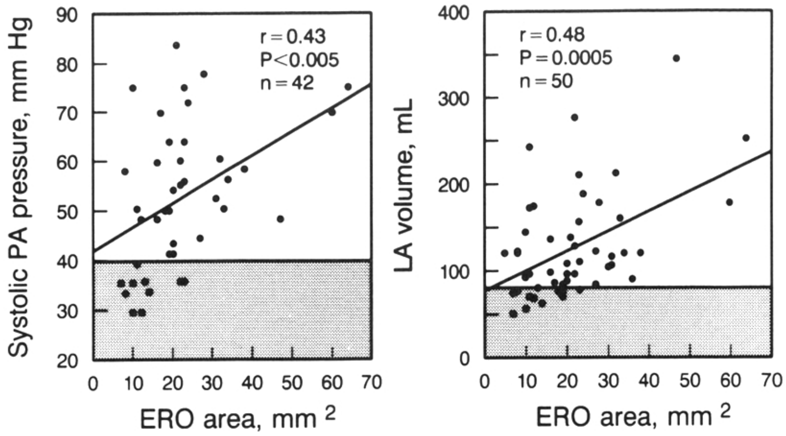


Figure 9. Ischemic/functional mitral regurgitation. Correlation between effective regurgitant orifice (ERO) area and systolic pulmonary artery (PA) pressure and left atrial (LA) volume. **Gray zone** corresponds to the upper limit of normal in 23 normal patients. Note that with increasing effective regurgitant orifice area, systolic pulmonary artery pressure and left atrial volume increased.

regurgitation was considered a severe lesion by the surgeon and severe dilation of the left ventricle or left atrium usually occurred; thus, these values of effective regurgitant orifice can be considered to indicate severe lesions.

Limitations of the study. Our measurements of the effective regurgitant orifice area cannot be correlated to any previously validated method of effective regurgitant orifice area measurement because, for all practical purposes, such previous data do not exist. Invasive measurement of the effective regurgitant orifice area in humans has been rapidly abandoned because dual-catheter measurements in valvular regurgitation are rarely used (44) and regurgitant flow measurements by angiography are subject to large errors (45).

Direct comparison of the effective regurgitant orifice area to the size of the defect has exceptionally (although successfully) been done experimentally on prosthetic defects (25) and is not possible in human or animal lesions (28). Thus, anatomic comparisons are limited.

However, our calculation is based on the simple hydrodynamic principle satisfactorily used for the calculation of aortic valve area in aortic stenosis (5,6). Mitral stroke volume measurement has been controversial, but validation studies have been performed at our institution with regard to both regurgitant volume (46) and regurgitant velocities (44). Most important, the value of effective regurgitant orifice area calculation is confirmed not only by the surgical evaluation of the lesion but also by the strong correlations to the hemodynamic consequences of the valve lesion.

Clinical perception of the severity of the valvular lesion as expressed by the effective regurgitant orifice area may be difficult, as with every new index, but will probably be attainable with continued use of the method.

Conclusions. The measurement of the effective regurgitant orifice area is a noninvasive Doppler development of an old hemodynamic concept that allows a direct measure of the lesion severity of mitral and aortic regurgitation. The feasibility of the method is excellent after the initial learning phase. The effective regurgitant orifice area is an important and clinically significant index of the severity of regurgitation. It brings additive information to the regurgitant volume and fraction, and the three measurements should be integrated in a comprehensive, noninvasive, quantitative assessment of mitral and aortic regurgitation.

We thank Jolene M. Bartelt for excellent secretarial support and Sara L. Helgeson for excellent data analysis support in the preparation of the manuscript.

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